10/561,075

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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WO 2005/078133 A3

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(21) International Application Number:
PCT/US2005/002362

(22) International Filing Date: 27 January 2005 (27.01.2005)

(25) Filing Language: English

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(30) Priority Data:
60/543,034 9 February 2004 (09.02.2004) US

(71) Applicant *(for all designated States except US)*: **MONSANTO TECHNOLOGY LLC** [US/US]; 800 North Lindbergh Boulevard, St. Louis, MO 63167 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **WANG, Tianlin** [US/US]; 5220 Dutch Elm Drive, Apex, NC 27539 (US). **LOHUIS, Michael, M.** [CA/US]; 12959 Beaver Dam Road, Des Peres, MO 63131 (US). **KOJIMA, Cheryl, J.** [US/US]; 117 Royal Heights Drive, Knoxville, TN 37920 (US). **DU, Fengxing** [CN/US]; 228 Country Hollow Court, St. Charles, MO 63304 (US). **BYATT, John, C.** [US/US]; 214 Country Creek Court, Ballwin, MO 63011 (US).

(74) Agent: **KAMMERER, Patricia, A.**; Howrey Simon Arnold & White, LLP, 2941 Fairview Park Drive, Box 7, Falls Church, VA 22042 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

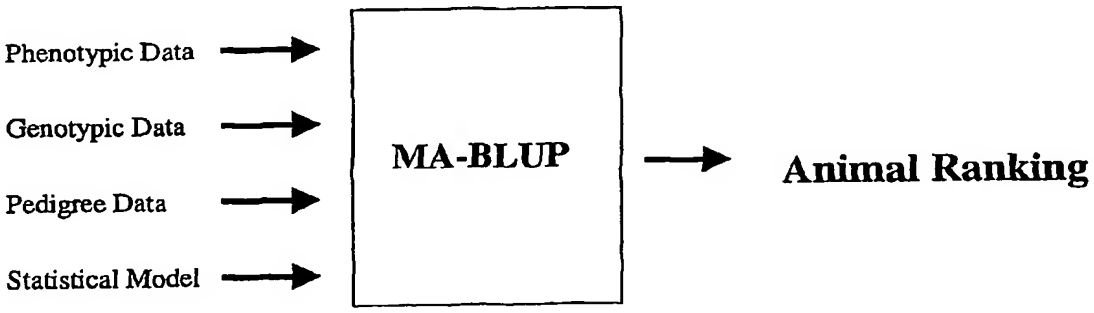
(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(88) Date of publication of the international search report:
16 March 2006

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: MARKER ASSISTED BEST LINEAR UNBIASED PREDICTED (MA-BLUP): SOFTWARE ADAPTIONS FOR PRACTICAL APPLICATIONS FOR LARGE BREEDING POPULATIONS IN FARM ANIMAL SPECIES



(57) Abstract: The invention provides methodologies for improved molecular genetic analysis of individual animals and animal populations. The invention includes methods and systems for identifying those animals in a population that are most likely to heritably pass on desirable traits. Provided are means for evaluating the estimated breeding values and increasing the average genetic merit for animals in a population. For each trait, the instant invention provides methods for evaluating the relative effect of one or more quantitative trait loci (QTL) and three or more molecular genetic markers for each QTL. The relationship between these various markers and the pre-selected trait and QTL is calculated, along with the contribution of other factors such as pedigree and known measures with respect to quantitative trait, and these data are used to calculate estimated breeding values for the animals in the herd and to rank the animals according to these estimated breeding values.

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INTERNATIONAL SEARCH REPORT

Application No
PCT/US2005/002362

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A01K67/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A01K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, BIOSIS, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MEUWISSEN T.: "Genomic selection: the future of marker assisted selection and animal breeding" ELECTRONIC FORUM ON BIOTECHNOLOGY IN FOOD AND AGRICULTURE, 17 October 2003 (2003-10-17), pages 54-59, XP002334468 Retrieved from the Internet: URL:http://www.fao.org/biotech/Torino.htm> page 55, paragraph 3 ----- -/--	1-7, 10-17, 20-30, 43-46

[X] Further documents are listed in the continuation of box C.

[ ] Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
12 August 2005	09. 12. 2005

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Chakravarty, A

INTERNATIONAL SEARCH REPORT

Application No
PCT/US2005/002362

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MEUWISSEN T H E ET AL: "Marker-assisted selection in animal breeding schemes" ANIMAL GENETICS, vol. 27, no. SUPPL. 2, 1996, page 101, XP009048356 & 25TH INTERNATIONAL CONFERENCE ON ANIMAL GENETICS; TOURS, FRANCE; JULY 21-25, 1996 ISSN: 0268-9146 abstract	1-7, 10-17, 20-30, 43-46
A	DEKKERS JACK C M ET AL: "Optimal selection on two quantitative trait loci with linkage." GENETICS, SELECTION, EVOLUTION. : GSE. 2002 MAR-APR, vol. 34, no. 2, March 2002 (2002-03), pages 171-192, XP002334470 ISSN: 0999-193X the whole document	

INTERNATIONAL SEARCH REPORT

application No.
PCT/US2005/002362

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-7, 10-17, 20-30, 43-46

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-7,10-17,20-30,43-46

Methods for ranking an animal population by using MA-BLUP to calculate the EBV based on data from databases of traits and corresponding QTLs and markers; systems for implementing these methods.

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2. claims: 8 (part) , 9, 18 (part), 19, 31, 34, 37 (part), 38 (part), 39, 40.

Methods/systems where at least one of the markers is an SNP in the PRKAG3 gene

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3. claims: 8 (part), 18 (part), 37 (part), 38 (part).

Methods/systems where at least one of the markers is an SNP in the porcine melanocortin-4-receptor gene

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Published:
— *with international search report*
— *with amended claims and statement*

(88) Date of publication of the international search report:
16 March 2006

Date of publication of the amended claims and statement:
20 April 2006

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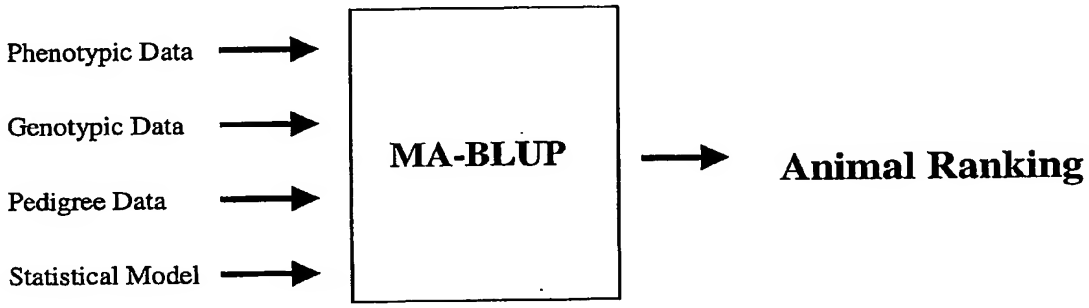
(54) Title: MARKER ASSISTED BEST LINEAR UNBIASED PREDICTED (MA-BLUP): SOFTWARE ADAPTIONS FOR PRACTICAL APPLICATIONS FOR LARGE BREEDING POPULATIONS IN FARM ANIMAL SPECIES



(57) Abstract: The invention provides methodologies for improved molecular genetic analysis of individual animals and animal populations. The invention includes methods and systems for identifying those animals in a population that are most likely to heritably pass on desirable traits. Provided are means for evaluating the estimated breeding values and increasing the average genetic merit for animals in a population. For each trait, the instant invention provides methods for evaluating the relative effect of one or more quantitative trait loci (QTL) and three or more molecular genetic markers for each QTL. The relationship between these various markers and the pre-selected trait and QTL is calculated, along with the contribution of other factors such as pedigree and known measures with respect to quantitative trait, and these data are used to calculate estimated breeding values for the animals in the herd and to rank the animals according to these estimated breeding values.

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AMENDED CLAIMS
Received by the International Bureau on 09 February 2006 (09.02.2006)

1. A method of increasing an animal population's average genetic merit, comprising;
   a. selecting one or more traits for which an improved genetic merit is desired:
   b. selecting one or more quantitative trait locus (QTL) for each selected trait;
   c. selecting three or more molecular genetic markers of interest for each QTL for each selected trait;
   d. providing databases comprising:
      i. genotype data for three or more molecular genetic markers for each selected trait, for a plurality of animals in the population;
      ii. data providing the pedigree for each animal in the population;
      iii. optionally, data for one or more fixed effects;
   e. using a computer program capable of performing a marker assisted best linear unbiased prediction to simultaneously analyze the data from the provided databases to calculate a ranking of the animals; wherein the computer program uses a variable-size block-diagonal preconditioned gradient (PCCG) algorithm to rank the animals; wherein the animals are ranked according to their estimated breeding value (EBV) for the selected molecular genetic markers and, if provided, quantitative traits.
2. The method of 1 further comprising using the calculated EBVs to prepare a breeding plan for the animal population that provides for optimal improvement in the genetic merit of the population.
3. The method of claim 1 wherein the animal population is a swine herd.
4. The method of claim 1 wherein the trait is selected from the group consisting of: efficient growth traits, meat quality traits, reproduction traits, and health traits.
5. The method of claim 1 wherein the molecular genetic markers are selected from any polymorphism known to affect expression of the mRNA or protein from a gene.
6. The method of claim 5 where the polymorphism is selected from the group consisting of: single nucleotide polymorphisms, simple sequence repeats, protein point mutations, and gene isoforms.

7. The method of claim 3 wherein at least one molecular genetic marker is selected from those markers known to modulate a favorable phenotype.

8. The method of claim 3 wherein at least one of the molecular genetic markers is a marker for selected from the group consisting of: a single nucleotide polymorphism in the porcine PRKAG3 (protein kinase, AMP-activated gamma-3 subunit) gene, and a polymorphism in the porcine melanocortin-4-receptor.

9. The method of claim 3 wherein at least one of the molecular genetic markers is a marker for a single nucleotide polymorphism in the porcine PRKAG3 gene.

10. The method of claim 1 wherein the computer program uses an iteration-on-data (IOD) algorithm.

12. The method of claim 1 wherein the output of the computer program further comprises results that indicate the informativeness of one or more of the selected molecular genetic marker for at least one quantitative trait locus (QTL) and/or a calculation of the genetic closeness/proximity of one or more molecular markers to at least one QTL.

13. The method of claim 12 wherein the molecular genetic markers having the highest degree of informativeness and/or closeness for at least one QTL are identified.

14. The method of claim 1 wherein the computer program utilizes a scripting feature to improve the ease of user interface.

15. The method of claim1 wherein the selected molecular genetic markers comprise a marker haplotype.

16. A system for increasing an animal population's average genetic merit for at one or more selected traits, the system comprising:

a. a computer;

b. a computer accessible database providing data on one or more quantitative trait locus (QTL) for each selected trait;

c. a computer accessible database providing data, for animals in population, for three or more molecular genetic markers for each selected QTL for each selected trait;

d. a computer accessible database providing pedigree data for animals in the population;

e. optionally, a computer accessible database providing individual data for each animal in the population for at least one fixed effect;

f. a computer program capable of performing marker-assisted best linear unbiased prediction and simultaneously evaluating the data in all databases and ranking the animals in the population according to their respective estimated breeding value for each of the selected traits; wherein the computer program uses a variable-size block-diagonal preconditioned gradient (PCCG) algorithm to rank the animals;

g. a user interface including a data entry system, said user interface coupled to said computer and configured to allow the user to instruct the computer to access the available databases and use the computer program to generate output that includes a ranking of the animals according to their estimated breeding values and/or their individual estimated breeding values.

17. The system of claim 16 wherein the animal population is a swine herd.

18. The system of claim 17 wherein at least one of the molecular genetic markers is selected from the group consisting of markers for the porcine PRKAG3 gene and the gene encoding the melanocortin-4-receptor.

19. The system of claim 17 wherein at least one of the molecular genetic markers is a marker for a single nucleotide polymorphism in the porcine PRKAG3 gene.

20. The system of claim 17 wherein the selected molecular genetic markers comprise a marker haplotype.

21. A system for identifying the molecular genetic marker(s) having the highest degree of informativeness for one or more selected quantitative trait locus (QTL), the system comprising:

a. a computer;

b. a computer accessible database providing individual data, for animals in population, for three or more molecular genetic markers for each selected quantitative trait locus;

c. a computer program capable of simultaneously evaluating the data in all databases and determining the relative informativeness for each of the molecular genetic markers for which data is provided; wherein the computer program is capable of performing marker-assisted best linear unbiased prediction and uses a variable-size block-diagonal preconditioned gradient (PCCG) algorithm to determine the relative informativeness of each molecular genetic marker;

d. a user interface including a data entry system, said user interface coupled to said computer and configured to allow the user to instruct the computer to access the available databases and use the computer program to generate output that includes a indication of the informativeness of each molecular genetic marker for which data was provided.

22. The system of claim 21 wherein the quantitative trait locus is selected from any locus known to be associated with a known trait.

23. The system of claim 21 wherein the quantitative trait locus is selected from any locus for traits selected from the group consisting of efficient growth traits, meat quality traits, reproduction traits, and health traits.

24. The system of claim 21 further comprising providing computer accessible database(s) containing individual data for animals in the population for at least one fixed effect; wherein the computer executable program is capable of simultaneously evaluating the data in all provided databases and ranking the animals in the population according to their respective estimated breeding value for each of the selected traits.

25. The system of claim 21 wherein the selected molecular genetic markers comprise a marker haplotype.

29. The method of claim 1 further comprising using the animals' ranks to identify the optimal breeding pairs in the population.

30. The method of claim 29 wherein the selected molecular genetic markers comprise a marker haplotype.

31. A method of enhancing one or more meat quality trait(s) in pigs, the method comprising:

a) screening a plurality of pigs to identify the nature of one or more single nucleotide polymorphisms (SNPs) in the porcine PRKAG3 gene, wherein said SNP(s) is/are selected from the group consisting of: an A/G at position 51, A/G at position 462, A/G at position 1011, C/T at position 1053, C/T at position 2475, A/G at position 2607, A/G at position 2906, A/G at position 2994, and C/T at position 4506, wherein all numbering is according to the sequence of SEQ ID NO:1 and identifying those having a desired allele;

b) selecting those pigs identified as having a desired allele;

c) using the selected pigs as sires/dams in a breeding plan to produce offspring; wherein the offspring have an increase frequency of the desired allele.

32. The method of claim 31 wherein the presence or absence of the polymorphism is determined by a method selected from the group consisting of: DNA sequencing, restriction fragment length polymorphism (RFLP) analysis, heteroduplex analysis, single strand conformational polymorphism (SSCP) analysis, denaturing gradient gel electrophoresis (DGGE), real time PCR analysis (TAQMAN®), temperature gradient gel electrophoresis (TGGE), primer extension, allele-specific hybridization, and INVADER® genetic analysis assays.

33. The method of claim 31 wherein at least one meat quality trait is selected from the group consisting of increased pH and decreased 7-day purge.

34. A kit for detecting the nature of one or more polymorphisms in the porcine PRKAG3) gene; the kit comprising a means for detecting for detecting the polymorphism in the DNA and or RNA from the gene;
wherein the polymorphisms are selected from the group consisting of one or more of the following SNP(s): an A/G at position 51, A/G at position 462, A/G at position 1011, C/T at position 1053, C/T at position 2475, A/G at position 2607, A/G at position 2906, A/G at position 2994, and C/T at position 4506, wherein all numbering is according to the sequence of SEQ ID NO:1.

35. The kit of claim 34 whereby the polymorphism is detected by one or more of the following means of detection: DNA sequencing, restriction fragment length polymorphism (RFLP) analysis; heteroduplex analysis, single strand conformational polymorphism (SSCP), denaturing gradient gel electrophoresis (DGGE), polymerase chain reaction (PCR), real time PCR analysis (TAQMAN®), temperature gradient gel electrophoresis (TGGE), enzyme linked immunosorbent assay (ELISA) and other immunoassay;
wherein the kit comprises one or more of the following: a restriction endonuclease enzyme, a DNA polymerase, a reverse transcriptase, a buffer, deoxyribonucleotides, an oligonucleotide suitable for use as a DNA or RNA probe, an oligonucleotide suitable for use as a primer in DNA or RNA synthesis, a fluorescent marker, and an antibody.

36. An oligonucleotide suitable for use in a kit according to claim 35.

37. The oligonucleotide of claim 36 selected from primers comprising the sequence of any of the primers listed in Table 1 (SEQ ID NO:2-17).

38. The oligonucleotide of claim 36 selected from the group consisting of the primers provided in Table 1 (SEQ ID NO:2-17).

STATEMENT UNDER ARTICLE 19 (1)

Claims 1, 10, 16, 21, 22, 29 and 30 are amended.

Claims 11, 26-28 and 39-46 are cancelled.

Claims 2-9, 12-15, 17-20, 23-25, 31-38 are unchanged.

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference 11916.0065.00PC00	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/US2005/002362	International filing date *(day/month/year)* 27 January 2005 (27.01.2005)	Priority date *(day/month/year)* 09 February 2004 (09.02.2004)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant MONSANTO TECHNOLOGY LLC		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 14 August 2006 (14.08.2006)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Dorothée Mülhausen e-mail: pt01@wipo.int

Form PCT/IB/373 (January 2004)

REC'D 12 DEC 2005
WIPO PCT

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet)	
Applicant's or agent's file reference see form PCT/ISA/220	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2005/002362	27.01.2005	09.02.2004

International Patent Classification (IPC) or both national classification and IPC
A01K67/02

Applicant
MONSANTO TECHNOLOGY LLC

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Chakravarty, A

Telephone No. +49 89 2399-8536

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed.

   ☒ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☒ not paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-7,10-17,20-30,43-46

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	10-17,20-30,43-46
	No:	Claims	1-7, 36, 41,42
Inventive step (IS)	Yes:	Claims	
	No:	Claims	10-17,20-30,43-46
Industrial applicability (IA)	Yes:	Claims	1-46
	No:	Claims	

2. Citations and explanations

   see separate sheet

Re Item IV

Lack of unity of invention

The application lacks unity as required by Art. 3(4)(iii) PCT and Rule 13 PCT:

Rule 13.1 PCT states that for unity of invention to be present, all subject-matter should be linked by a single general inventive concept.

1: methods for ranking an animal population by using MA-BLUP to calculate the EBV based on data from database of traits and corresponding QTLs and markers; systems for implementing these methods. - Claims 1-7,10-17,20-30,43-46

2: methods/systems where at least one of the markers is an SNP in the PRKAG3 gene - claims 8 (part) , 9, 18 (part), 19, 31, 34, 37 (part), 38 (part), 39, 40.

3: methods/systems where at least one of the markers is an SNP in the porcine melanocortin-4-receptor gene - claims 8 (part), 18 (part), 37 (part), 38 (part).

The common concept (technical relationship) linking these Groups together is that they all require the use a computer (programme) to carry out a method for ranking a population of animals according to a estimated breeding value EBV) by performing a marker assisted best linear unbiased prediction to simultaneously analyse the data from the provided databases to calculate a ranking of the animals; wherein the animals are ranked according to their estimated breeding value (EBV) for the selected molecular genetic markers and, if provided, quantitative traits.
However, this concept cannot be regarded as the "single general inventive concept" required by Rule 13.1 PCT because the automation of known methods cannot confer an inventive step.

D1 (Meuwissen T, MAS workshop 2003) is a review of marker assisted selection in animal breeding. On page 55 (paragraph 3), the use of QTL regions and markers in and surrounding them are used in a method for calculating EBV in BLUP breeding value estimation. The only apparent difference between D1 and the presently claims subject-matter is that the claim explicitly requires that a computer programme is used to perform the analysis.

The requisite unity of invention therefore no longer exists and *search* is carried out for the 'invention' first mentioned in the claims (Group 1).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The present application concerns a method for ranking a population of animals according to a estimated breeding value EBV) which is calculated using a computer program capable of performing a marker assisted best linear unbiased prediction to simultaneously analyse the data from the provided databases to calculate a ranking of the animals; wherein the animals are ranked according to their estimated breeding value (EBV) for the selected molecular genetic markers and, if provided, quantitative traits.

Aside from problems of lack of clarity, the present claims appear to lack novelty and inventive step.
(Reference is made to the following document/s/:
D1: Meuwissen T, MAS workshop 2003.

D1 is a review of marker assisted selection in animal breeding. On page 55, the use of QTL regions and markers in and surrounding them in a method for calculating EBV in BLUP breeding value estimation. The only apparent difference between D1 and the presently claims subject-matter is that the claim explicitly requires that a computer programme is used to perform the analysis. The use of computers to perform calculations is so routine that it can be regarded as implicitly disclosed in the prior art.
In any case, it cannot be taken as conferring inventive step since the performance of calculations using an computer is routine.
Claims 1-7 lack novelty. Claims 10-17,20-30,43-46 lack inventive step.
Claim 36 lacks novelty because it reads on known oligonucleotides.
Claims 41-42 lacks novelty because it reads on known animals.